REMARKS

I. Claim Amendments

Claims 1-5, 7-20, 22-33 and 68 are pending in the present application and were examined. Claim 6 is cancelled. Claims 34-67, 69 and 70 are withdrawn. Applicants amended claim 1 to recite that the claimed device includes a single calibration zone. Basis for this amendment can be found in the specification, considered as a whole, e.g., in Figure 4 and at page 29, line 18, to page 30, and line 10.

II. Claim Rejections 35 U.S.C. §112

Claim 6 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite because, allegedly, it was not clear how the fourth zone and the fifth zones are overlapping, if a calibration zone is placed between these two zones. Office Action, page 2.

Applicants continue to assert that claim 6 was definite, for all the reasons previously discussed. Nonetheless, in the interest of expediting prosecution, Applicants canceled claim 6. Thus, this rejection is moot.

III. Rejections Under 35 U.S.C. Section §103

A. Claims 1-3, 5, 9-13, 20, 22-25, 28, 30-33 and 68 are not obvious over Good et al., in view of Wei et al. or Robinson et al.

Claims 1-3, 5, 9-13, 20, 22-25, 28, 30-33 and 68 were rejected under 35 U.S.C. § 103(a) in view of Good et al. (US Patent 6,194,224) (which may also be referred to herein as "Good"), in combination with Wei et al. (US 2003/0119203) (which may also be referred to herein as "Wei") or Robinson et al. (US 5,726,064) (which may also be referred to herein as "Robinson").

In summary, the rejection was premised on the assertion that Good et al. disclose a device of several different specifically described zones, which have various compositions, with some of the zones overlapping with each other. It was stated that Good et al. differ from Applicants' invention in failing to teach a calibration zone comprising an immobilized binding agent having

an affinity for the labelled non-immobilized molecule. Office Action, page 4. Wei et al. and Robinson et al. were relied upon to compensate for this deficiency.

It was also stated that the recitation "wherein the amount of the analyte present in the sample is calculated from a signal obtained in the fourth zone and a signal obtained in the calibration zone" does not further limit the claims directed to a device. Office Action, page 6. It was asserted that this recitation is directed to intended use of the device, which "...must result in a structural difference between the claimed invention and the prior art..." to patentably distinguish Applicant's claimed invention from the prior art. It was alleged that the combination of references teaches the same structural limitations as defined by Applicants' claims and thus the combination of references reads on the claimed invention. Office Action, pages 6-7.

Applicants respectfully traverse this rejection for the reasons discussed below.

Applicants submit that a person of ordinary skill in the field of endeavour of Applicants' claimed invention would find no reason, motivation or suggestion in the aforementioned references to combine the teachings of Good et al. with Wei et al. and/or Robinson et al. to achieve the Applicants' claimed device.

Good et al. disclose a device comprising a porous material having a sample receiving zone, a reagent zone containing antibodies labelled with colloid gold particles, and a detection zone containing immobilised molecules of the specified analyte when a membrane of the device is moist. Downstream from the detection zone, the device described by Good et al. comprises a control zone which indicates the presence of a sample by a detectable change, e.g., visible change. Col. 3, lines 16-19.[1] As is apparent from column 6, lines 53-67, Good et al. disclose a positive/negative test and do not determine the amount of a certain analyte. In the above paragraph it is stated that "*...a positive sample will inhibit the formation of a visible line in the test zone...*" and that "*Normally a negative oral fluids sample will produce two colored lines, one in the test zone region and one in the control zone region and a positive oral fluids sample will show only one line in the control zone region.*"

[1] In the Response and Amendment filed on May 15, 2007, at page 12, Applicants inadvertently stated that Good et al. disclose a calibration zone. As is clear from Good et al.'s disclosure and the discussion above, Good et al. do not disclose a calibration zone. Thus, Applicants withdraw that statement.

As correctly pointed out in the Office Action, Good et al. fail to disclose a calibration zone, much less a single calibration zone comprising an immobilized binding agent having an affinity for the labelled non-immobilized molecule capable of specifically binding to the analyte to be assayed, as required by Applicants' claim 1 (and all claims dependent from claim 1). Good et al. also do not disclose a device for the quantitative determination of an analyte in a sample, wherein the content of the analyte present in the sample is calculated from a signal obtained in the test zone and a signal obtained in the calibration zone. Applicants respectfully traverse the assertion in the Office Action that these functional recitations are directed to intended use of the device, and thus, in effect are not considered in determining patentability of Applicants' claims.

Section 2173.05(g) of the MPEP states that

> A functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used. A functional limitation is often used in association with an element, ingredient, or step of a process to define a particular capability or purpose that is served by the recited element, ingredient or step. >In *Innova/Pure Water Inc. v. Safari Water Filtration Sys. Inc.*, 381 F.3d 1111, 1117-20, 72 USPQ2d 1001, 1006-08 (Fed. Cir. 2004), the court noted that the claim term 'operatively connected' is 'a general descriptive claim term frequently used in patent drafting to reflect a functional relationship between claimed components,' that is, the term 'means the claimed components must be connected in a way to perform a designated function'. 'In the absence of modifiers, general descriptive terms are typically construed as having their full meaning.' *Id.* at 1118, 72 USPQ2d at 1006.
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> In a claim that was directed to a kit of component parts capable of being assembled, the Court held that limitations such as 'members adapted to be positioned' and 'portions . . . being resiliently dilatable whereby said housing may be slidably positioned' serve to precisely define present structural attributes of interrelated component parts of the claimed assembly. *In re Venezia*, 530 F.2d 956, 189 USPQ 149 (CCPA 1976).

Thus, Applicants respectfully submit that all of Applicants' claims limitations must be considered in determining patentability of the claims.

Applicants also respectfully traverse the assertion that Wei et al., Robinson et al. and the remaining references relied upon in the Office Action supply the deficiencies of Good et al. to render obvious Applicants' claims.

Wei et al. disclose a lateral flow device for determining an analyte in a sample using the "sandwich" assaying technique. The lateral flow device according to Wei et al. comprises a sample pad, a conjugate pad, typically containing probes 41 and probe conjugates 42 in such form that the probe conjugates are available for bonding with an analyte. See paragraph 0031. The device further comprises a detection zone which may have an immobilized capture reagent, such as an antibody. Paragraphs 0010 and 0011. The device may comprise a calibration zone, which comprises two or more (e.g. three, four or more) control lines. (See Figures 1, 1A and 1B, paragraphs [0012] and [0039], and claim 1 section (b)(ii) stating that the "*...calibration zone comprising at least first and second control lines,.....*".) The amount of the analyte may be determined by comparing the intensity level of a detection line 24 generated at the detection zone 31 with the intensity level of the calibration lines to calculate the amount of the analyte present. *See*, e.g., paragraph [0039]. Example 3 indicates that the intensities in the three calibrations lines are 0.54 ng, 5.4 ng and 54 ng analyte, respectively. The concentration of analyte of an unknown sample could then be visually determined by comparing the intensity level of the detection line with the intensity level of the three calibration lines. Paragraph 0039.

Thus, Wei et al. disclose an assay device for the semi-quantitative determination of an analyte in a sample which provides an approximate value of the analyte, based on comparison of a detection line intensity level with the intensity level of two or more calibration lines.

Robinson et al. describe a device for determining a ligand in a sample, similar to that of Wei et al. In column 3, lines 55-58, it is stated that, for a quantitative method, the number of auxiliary calibration surfaces is preferably greater than one and more preferably greater than or equal to four. Applicants submit that it is known in the art that calibration surfaces are equivalent to calibration zones. In Robinson et al. the calibration zone or zones utilize a movable second specific binding reagent which binds in the calibration zone(s) (e.g. see claims 2, 6 and 7). The calibration zone(s) described by Robinson et al. use a different technique than the calibration zone described in the present invention as the present invention only relates to one mobile specific binding reagent.

Thus, Robinson et al. disclose the use of two movable specifically binding molecules, one for the binding in the measurement zone and one for binding in the control zone(s) for the semi-quantitative or quantitative determination of a ligand in a sample.

In contrast, Applicants' claimed invention relates to an analytical device for the quantitative determination of an analyte in a sample. Applicants' device comprises a first zone (which also may be referred to herein as "an application zone"), onto which an analyte sample can be applied, and a second zone (which may be referred to herein as a "conjugate zone") comprising a non-immobilized molecule (e.g., an antibody) capable of binding specifically to the analyte of interest present in the sample. The conjugate zone also includes a detectable label.

Downstream from the conjugate zone is a fourth zone (also referred to herein as a "test zone"), comprising a molecule of the same type as the one to be assayed or an analogue thereof in an immobilized state. A single calibration zone is located downstream from the test zone. The single calibration zone comprises an immobilized binding agent (e.g., an antibody) having an affinity for the labelled non-immobilized molecule capable of binding specifically to the analyte to be assayed. The amount of the analyte present in the sample is determined from a signal obtained in the fourth zone and a signal obtained in the calibration zone.

It is well established that all claim limitations must be considered in judging patentability of the claimed invention over prior art. *In re Wilson*, 165 USPQ 494 (CCPA 1970). This includes functional limitations, as discussed above.

The construction and function of the Applicants' device is significantly and fundamentally different from that of Good et al., at least because Good et al.'s device lacks the calibration zone and because it does not measure the amount of the analyte, but measures only the presence or absence of the analyte. Thus, Good et al.'s device is a positive/negative test device.

The devices of Wei et al. and Robinson et al. are also significantly distinct and different from Applicants' claimed device for the reasons set forth above. In summary, Wei et al. relate to a device performing a semi-quantitative test (wherein the intensity level of the test line is compared to the more than one calibration lines) and the device described by Robinson et al.

relates to a semi-quantitative or a quantitative test using two different movable specifically binding molecules, one for the binding in the measurement zone and one for binding in the control zone(s). In contrast, Applicants' claimed device is directed to a quantitative test giving the content of the analyte of interest using only one movable specifically binding molecule for the binding in the measurement zone and in the control zone. \

The problem solved by Applicants' invention is to provide a device which makes it possible to monitor small day-to-day changes in the level of an analyte of interest on a daily basis or during selected time intervals in a cost-effective, highly sensitive, reproducible, and precise manner, which requires a minimum of handling steps and which is easy to perform.

None of the cited prior art documents solves or touches upon the problem solved by the Applicants' invention. Furthermore, the information provided in the cited documents cannot be used by a skilled person to solve the problem solved by the Applicants' invention.

None of the references relied upon suggest a specific need for a design, nor a specific focus in the market, on lateral flow devices which solve the problem solved by the claimed invention. Furthermore, there is a significant number of combinations of designs, detection techniques, construction techniques and algorithms available in the combination of the three references from which a person of ordinary skill in the art would have to selectively pick a particular combination of features (with no guidance in the references to do so) in an effort to obtain Applicants' claimed device.

Therefore, a person skilled in the art would have no reason, based on the cited references to arrive at the combination of features to provide the quantitative test device defined in the Applicants' claims, which solves the problem of the present invention.

Accordingly, claim 1 is not obvious under 35 U.S.C. §103.

B. Claims 2-5, 7-20, 22-33 and 68 are not obvious over Good et al., Wei et al., Robinson et al., in view of Polzius et al., Schlipfenbacher et al., Davis et al., Lee et al., Henderson et al., Robinson et al., Frushour et al. or Sundrehagen.

Claims 4 and 6 were rejected as obvious over Good et al. in view of Polzius et al. (U.S. Patent

6,130,097) (also referred to herein as "Polzius ") or Schlipfenbacher et al. (U.S. Patent 5,160,486) (also referred to herein as "Schlipfenbacher"). The rejection of claim 6 is moot due to cancellation of this claim. It was alleged that Polzius teaches that it is known in the art to overlap zones on a test strip to provide for fluid contact of the zones. Schlipfenbacher was cited for its alleged teaching that overlapping zones on a test strip are known in the art. It was concluded that it would have been obvious to combine Good et al. with Polzius et al. and Schlipfenbacher et al. to obtain the device of claim 4 with overlapping zones.

The remaining claims, rejected as obvious, were similarly rejected by combining Good et al. with other references as follows:

- Claims 7 and 8: over Good et al., Wei et al., or Robinson et al. in view of Davis et al. (U.S. Patent 6,352,862) (also referred to herein as "Davis") because allegedly Davis et al.'s teaching of several labeled specific binding reagents and multiple capture reagents, combined with Good et al. would have made claims 7 and 8 obvious.

- Claims 14-16: over Good et al., Wei et al., or Robinson et al. in view of Lee et al. (WO 02/04671) (also referred to herein as "Lee") because allegedly Lee's disclosure of bovine serum albumin (BSA), used as a spacer, combined with Good et al. would have made obvious incorporating spacer molecules, including BSA, into Good et al.'s device, thereby rendering claims 14-16 obvious.

- Claim 17: over Good et al. and Wei et al. in view of Lee et al., and Henderson et al. (U.S. 2004/0072248) (also referred to herein as "Henderson") based on Henderson's alleged teaching of carboxymethyloxime (CMO) conjugated to bovine serum albumin and to an estrogen, and used as a binding substance, immobilized on the surface of a test strip and used in assays. It was reasoned that it would have been obvious to incorporate CMO into Good's modified device to render *prima facie* obvious claims 14-16.

- Claims 18 and 19: Over Good et al. and Wei et al. or Robinson et al. in view of Frushour et al. (US 2003/0059951) (also referred to herein as "Frushour ") because Frushour's alleged teaching of the spatial separation zones on a test strip and the flow rate characteristics of the porous solid phase material can be selected to allow adequate

reaction times in which the necessary specific binding can occur, and allow the labeled antibody in the labeled antibody zone to dissolve through the porous solid phase material. It was asserted that a person of ordinary skill in the art would have found it obvious to combine teachings of the references, to achieve the device of Good et al. with a changed length of the third zone.

- Claims 26, 27 and 29: over Good et al. and Wei et al. and Robinson et al. in view of Sundrehagen (U.S. 6,716,641) (also referred to herein as "Sundrehagen") based on Sundrehagen's alleged teaching of using reagents in zones of a test strip. According to the Office Action, Sundrehagen discloses that the use of the reagents prevents non-specific binding of the detector reagent and/or analyte.

Applicants do not concede that characterization of the references in the Office Action is correct. Even if, arguendo, it were correct, Applicants submit that, these rejections are misplaced as a matter of law.

One test for a proper obviousness rejection requires the finding of some teaching, suggestion or motivation provided by the prior art, to combine the teachings of the prior art. The Office Action failed to establish such teaching, suggestion or motivation in the prior art.

While the Supreme Court in *KSR International Co. v. Teleflex Inc.,* 127 S.Ct.1727, 82 USPQ 2d 1385 rejected the use of the teaching/suggestion/motivation (TSM) test as the only test for obviousness analysis, it did not eliminate it as a possible test. The Court recognized that a showing of teaching, suggestion or motivation to combine the prior art elements to meet the claimed subject matter could provide a helpful insight in the determination of whether the claim(s) under consideration are obvious. Furthermore, the Court held that the obviousness analysis needs to be explicit and cannot be sustained by mere conclusory statements. According to the Court, a patent claim directed to several elements is not obvious based on a mere showing that each of the elements is known in prior art, and that a reason needs to be identified for prompting a person of ordinary skill to combine the prior art elements in the same way that the claimed invention does.

All obviousness rejections in the Office Action are based on selectively picking isolated elements of several prior art disclosures and combining them into a mosaic resembling Applicants' invention. There is no showing of a rational underpinning as to why a person of ordinary skill, aware only of the prior art (but not Applicants' claimed invention), would have known to:

1) choose such specific elements; and
2) combine them in the precise manner needed to obtain Applicants' claimed invention.

For all these reasons Applicants' respectfully request withdrawal of all obviousness rejections.

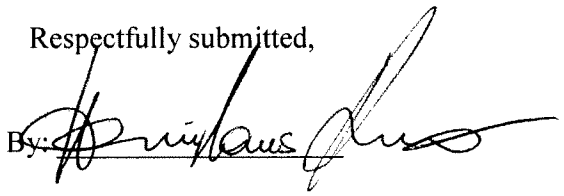
IV. Request for Allowance

Applicants respectfully submit that all claims are in condition for allowance, an indication of which is solicited.

In the event that any outstanding issues remain, Applicants respectfully request the courtesy of a telephone call to the undersigned counsel to resolve such issues in an expeditious manner and place the application in condition for allowance.

In the event that any variance exists between the fees enclosed herewith and those deemed necessary by the U.S. Patent and Trademark Office to enter and consider this amendment and response, or to maintain the present application pending, please credit or charge such variance to the undersigned Deposit Account Number 50-2478.

Respectfully submitted,

By: 

Date: October 24, 2007

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